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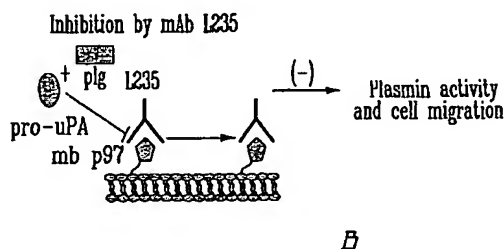
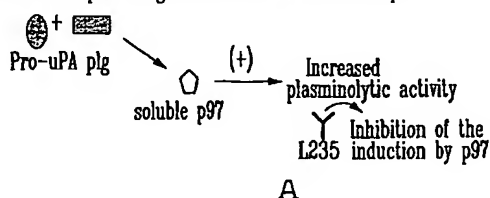
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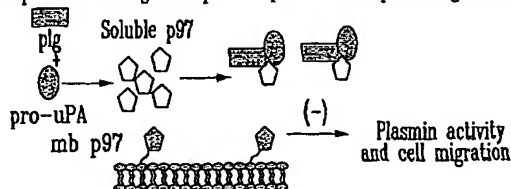
[Continued on next page]

(54) Title: **COMPOUND AND METHOD FOR REGULATING PLASMINOGEN ACTIVATION AND CELL MIGRATION**

Pro-uPA and plasminogen interaction with soluble p97



Competition of exogenous p97 for pro-uPA and plasminogen interaction



(57) Abstract: The invention relates to novel regulators of plasminogen activation and their use for regulating cell migration, plasminolysis, angiogenesis, fibrinolysis, for treating cancer and thrombo-embolic diseases such as heart stroke. Furthermore, the present invention relates to novel pharmaceutical compositions regulating cell migration, plasminolysis, angiogenesis and for treating cancer. In particular, the present invention relates to a method of regulating the activation of plasminogen comprising contacting a solution of pro-urokinase (uPA) or tissue plasminogen activator (tPA) and plasminogen with melanotransferrin (p97) for a time sufficient to effect regulation thereof.



MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

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# INTERNATIONAL SEARCH REPORT

International Application No  
PCT/CA2004/000697

**A. CLASSIFICATION OF SUBJECT MATTER**  
IPC 7 A61K38/40

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)  
IPC 7 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, BIOSIS, Sequence Search

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	<p>SALA ROBERTA ET AL: "The human melanoma associated protein melanotransferrin promotes endothelial cell migration and angiogenesis in vivo." EUROPEAN JOURNAL OF CELL BIOLOGY, vol. 81, no. 11, November 2002 (2002-11), pages 599-607, XP009037961 ISSN: 0171-9335 Results: "MTf induces an angiogenic response in the chick embryo CAM", "Induction of endothelial cell migration by MTf is partly dependent on VEGF"; Discussion: Last paragraph</p> <p style="text-align: center;">----- -/--</p>	<p>4-7, 10-17, 22, 24-27, 29, 32-41</p>

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

### \* Special categories of cited documents:

- \*A\* document defining the general state of the art which is not considered to be of particular relevance
- \*E\* earlier document but published on or after the international filing date
- \*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- \*O\* document referring to an oral disclosure, use, exhibition or other means
- \*P\* document published prior to the international filing date but later than the priority date claimed

- \*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- \*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- \*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- \*Z\* document member of the same patent family

Date of the actual completion of the international search

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International Application No  
PCT/CA2004/000697

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 6 455 494 B1 (JEFFERIES WILFRED A ET AL) 24 September 2002 (2002-09-24)  paragraphs '0027!, '0028!, '0037!, '0130!, '0201!, '0203!, '0237!, '0458!	4-7, 10-17, 22, 24-27, 29, 32-41
P,X	DEMEULE MICHEL ET AL: "Regulation of plasminogen activation: A role for melanotransferrin (p97) in cell migration." BLOOD, vol. 102, no. 5, 1 September 2003 (2003-09-01), pages 1723-1731, XP002300165 ISSN: 0006-4971 Results, page 1723, right-hand column, paragraph 2 - page 1724, left-hand column, paragraph 1	1-41, 43-46, 48-51
A	ROSE T M ET AL: "PRIMARY STRUCTURE OF THE HUMAN MELANOMA-ASSOCIATED ANTIGEN P97 (MELANOTRANSFERRIN) DEDUCED FROM THE MRNA SEQUENCE" PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF USA, NATIONAL ACADEMY OF SCIENCE. WASHINGTON, US, vol. 83, March 1986 (1986-03), pages 1261-1265, XP002934311 ISSN: 0027-8424 figure 3	1-54
Y	US 2002/119095 A1 (BROOKS ROBERT CHARLES ET AL) 29 August 2002 (2002-08-29)  paragraph '0077!	6, 7, 12, 13, 25, 26, 34, 35
A	SCHLINGEMANN R O ET AL: "EXPRESSION OF THE HIGH MOLECULAR WEIGHT MELANOMA-ASSOCIATED ANTIGEN BY PERICYTES DURING ANGIOGENESIS IN TUMORS AND IN HEALING WOUNDS" AMERICAN JOURNAL OF PATHOLOGY, vol. 136, no. 6, 1990, pages 1393-1406, XP009037870 ISSN: 0002-9440 page 1403, left-hand column, paragraph 1	16, 17, 39-41, 46, 51

# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/CA2004/000697

## Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:  
Rule 39.1(iv) PCT - Method for treatment of the human or animal body by therapy
2. ☐ Claims Nos.:  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this International application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; It is covered by claims Nos.:

### Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No  
PCT/CA2004/000697

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 6455494	B1	24-09-2002	
		US 5981194 A	09-11-1999
		US 2003077693 A1	24-04-2003
		US 2002119095 A1	29-08-2002
		AU 4553793 A	31-01-1994
		CA 2139862 A1	20-01-1994
		DE 69331100 D1	13-12-2001
		DE 69331100 T2	14-08-2002
		EP 0651768 A1	10-05-1995
		AT 269545 T	15-07-2004
		AU 717198 B2	23-03-2000
		AU 6783496 A	19-03-1997
		CA 2230372 A1	06-03-1997
		WO 9708560 A1	06-03-1997
		CN 1198214 A	04-11-1998
		DE 69632734 D1	22-07-2004
		EP 0847530 A1	17-06-1998
		IL 123441 A	11-01-2001
		JP 11511257 T	28-09-1999
		JP 3259963 B2	25-02-2002
		NZ 315997 A	30-08-1999
		WO 9401463 A1	20-01-1994
		EP 1018343 A1	12-07-2000
		EP 1143253 A1	10-10-2001
US 2002119095	A1	29-08-2002	
		US 6455494 B1	24-09-2002
		US 5981194 A	09-11-1999
		US 2003077693 A1	24-04-2003
		AT 269545 T	15-07-2004
		AU 717198 B2	23-03-2000
		AU 6783496 A	19-03-1997
		CA 2230372 A1	06-03-1997
		WO 9708560 A1	06-03-1997
		CN 1198214 A	04-11-1998
		DE 69632734 D1	22-07-2004
		EP 0847530 A1	17-06-1998
		IL 123441 A	11-01-2001
		JP 11511257 T	28-09-1999
		JP 3259963 B2	25-02-2002
		NZ 315997 A	30-08-1999
		AU 4553793 A	31-01-1994
		CA 2139862 A1	20-01-1994
		WO 9401463 A1	20-01-1994
		DE 69331100 D1	13-12-2001
		DE 69331100 T2	14-08-2002
		EP 1018343 A1	12-07-2000
		EP 1143253 A1	10-10-2001
		EP 0651768 A1	10-05-1995
		AU 8374001 A	25-02-2002
		AU 8502001 A	25-02-2002
		WO 0213843 A2	21-02-2002
		WO 0213873 A2	21-02-2002